Citation:

Olsen SF, Halldorsson TI, Willett WC, Knudsen VK, Gillman MW, Mikkelsen TB, Olsen J; NUTRIX Consortium. Milk consumption during pregnancy is associated with increased infant size at birth: prospective cohort study. *Am J Clin Nutr.* 2007 Oct;86(4):1104-10.

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Study Design:

Prospective Cohort Study

Class:

B - Click here for explanation of classification scheme.

Research Design and Implementation Rating:

NEUTRAL: See Research Design and Implementation Criteria Checklist below.

Research Purpose:

To examine whether milk consumption during pregnancy is associated with greater infant size at birth in a large prospective Danish pregnancy cohort.

Inclusion Criteria:

- Women were recruited in early pregnancy

Exclusion Criteria:

Not mentioned.

Description of Study Protocol:

Recruitment : Women were recruited while in early pregnancy during January 1997 to October 2002. Data were retrieved from questionnaires, telephone interviews, and registry linkages.

Design: Prospective cohort study

Blinding used (if applicable): not applicable

Intervention (if applicable): not applicable

Statistical Analysis:

- Potential confounding were adjusted by multiple linear regression for continuous outcomes and logistic regression for dichotomous outcomes.
- Covariates used in the models: infant gestational age, infant's sex, mother's parity, age, height, prepregnant BMI, gestational weight gain, smoking status, total energy intake,

father's height, family's socioeconomic status.

Data Collection Summary:

Timing of Measurements:

- Food frequency questionnaires were measured twice at approximately 25 and 35 weeks of gestation; the second time it was completed by only a group of 100 women.
- Weight, length, head circumference, abdominal circumference, and placental weight were measured at birth.
- Gestational age at birth was assessed from the last menstrual period or based on information on the expected date of delivery.

Dependent Variables

- Birth weight was measured right after birth and growth references provided by the British Child Growth Foundation were used to identify infants with a birth weight below or above the gestational age and sex specific 10th and 90th percentiles, respectively
- Birth length was measured from vertex to heel with legs stretched
- Head circumference corresponds to "hat measure"
- Abdominal circumference was measured just above the navel
- Placenta weight included membranes and umbilical cord

Independent Variables

- Milk consumption- it was recorded in eight questions in the FFQ where two of these referred to consumption of yogurt and six to consumption of milk. One glass of milk was estimated to be 200mL and one portion of yogurt to 150mL. Dairy products were quantified other than cheese and ice cream. Consumption of milk and its constituents was also quantified on the basis of standard portion sizes and food-composition tables. The FFQ was validated against dietary records and biomarkers of particular nutrients, but not specifically of milk or milk components

Control Variables

Description of Actual Data Sample:

Initial N: 101,042 registered in the DNBC, of whom 70,187 completed the FFQ

Attrition (final N): 50,117

Reasons for exclusion: FFQ not completed (30,855); Twinning, preterm, postterm delivery (13,834); Abnormally low or high energy intake (290); Missing birth weight (218); later births (5728).

Age: mean age: 29.1 ± 4.3

Ethnicity: not mentioned

Other relevant demographics: The percentage of smokers and women with low education level tended to exhibit a U-shaped relation.

Anthropometrics: Prepregnant BMI was the same for all categories of milk intake.

Location: Denmark

Summary of Results:

Key Findings

- Mean consumption of milk was 3.1 ± 2.0 glasses per day.
- Odds ratios for the risk of small-for-gestational age (SGA) birth according to frequency of milk intake: The odds declined with increasing consumption of milk. Women consuming >6 glasses of milk/d had a 49% (95%CI: 35%,61%) lower adjusted odds of having an SGA infant when compared with women with no milk intake. Nevertheless women who reported consuming > 6 glasses of milk/d had a 59% (95%CI:16%, 116%) higher odds of having a large-for-gestational age infant (P for trend < 0.001).
- Mean abdominal circumference,placental weight, head circumference and birth length all increased across the whole range of milk intake (*P* for trend <0.001). After adjustment for confounding, the total increments were 0.52cm, 26.4g, 0.13cm and 0.31cm for the four measures, respectively.
- No association was found between birth weight and fat from dairy products (excluding cheese and ice cream). However birth weight showed a relation with protein from dairy products;*P* for trend <0.001.
- Birth weight was constant across quintiles of nondairy protein. Cheese protein predicted a slight increase in birth weight (*P* for trend=0.23).
- In the univariate analysis, mean birth weight was ≥ 100 g higher among the group that consumed 4–5 glasses of milk/d compared with those who consumed no milk. Above that level no further increments were seen. When adjusted for potential confounders, a similar maximal increment was observed, but the rise tended to be graded across a broader exposure range, from 0 to ≥6 glasses of milk/d.

Author Conclusion:

Milk intake in pregnancy was associated with higher birth weight for gestational age, lower risk of small-for-gestational age, and higher risk of large-for-gestational age.

Reviewer Comments:

- *Exclusion of elegible women to participate in the study might have caused selection biases. Only 30 to 40% of pregnant women in the country were recruited.*
- *Another important limitation was the milk intake measurement made only during one month in midpregnancy which can give a distorted figure of the real consumption of milk for all periods of pregnancy.*
- *The results were restricted to singletons and term birth infants.*

Research Design and Implementation Criteria Checklist: Primary Research

Relevance Questions

1.	Would implementing the studied intervention or procedure (if found successful) result in improved outcomes for the patients/clients/population group? (Not Applicable for some epidemiological studies)	Yes
2.	Did the authors study an outcome (dependent variable) or topic that the patients/clients/population group would care about?	Yes
3.	Is the focus of the intervention or procedure (independent variable) or topic of study a common issue of concern to nutrition or dietetics practice?	Yes
4.	Is the intervention or procedure feasible? (NA for some epidemiological studies)	Yes

Validity Questions

1.	**Was the research question clearly stated?**	Yes
1.1.	Was (were) the specific intervention(s) or procedure(s) [independent variable(s)] identified?	Yes
1.2.	Was (were) the outcome(s) [dependent variable(s)] clearly indicated?	Yes
1.3.	Were the target population and setting specified?	Yes
2.	**Was the selection of study subjects/patients free from bias?**	No
2.1.	Were inclusion/exclusion criteria specified (e.g., risk, point in disease progression, diagnostic or prognosis criteria), and with sufficient detail and without omitting criteria critical to the study?	No
2.2.	Were criteria applied equally to all study groups?	N/A
2.3.	Were health, demographics, and other characteristics of subjects described?	No
2.4.	Were the subjects/patients a representative sample of the relevant population?	No
3.	**Were study groups comparable?**	N/A
3.1.	Was the method of assigning subjects/patients to groups described and unbiased? (Method of randomization identified if RCT)	N/A
3.2.	Were distribution of disease status, prognostic factors, and other factors (e.g., demographics) similar across study groups at baseline?	N/A
3.3.	Were concurrent controls used? (Concurrent preferred over historical controls.)	N/A
3.4.	If cohort study or cross-sectional study, were groups comparable on important confounding factors and/or were preexisting differences accounted for by using appropriate adjustments in statistical analysis?	N/A

3.5.	If case control or cross-sectional study, were potential confounding factors comparable for cases and controls? (If case series or trial with subjects serving as own control, this criterion is not applicable. Criterion may not be applicable in some cross-sectional studies.)	N/A
3.6.	If diagnostic test, was there an independent blind comparison with an appropriate reference standard (e.g., "gold standard")?	N/A
4.	**Was method of handling withdrawals described?**	???
4.1.	Were follow-up methods described and the same for all groups?	N/A
4.2.	Was the number, characteristics of withdrawals (i.e., dropouts, lost to follow up, attrition rate) and/or response rate (cross-sectional studies) described for each group? (Follow up goal for a strong study is 80%.)	Yes
4.3.	Were all enrolled subjects/patients (in the original sample) accounted for?	No
4.4.	Were reasons for withdrawals similar across groups?	N/A
4.5.	If diagnostic test, was decision to perform reference test not dependent on results of test under study?	N/A
5.	**Was blinding used to prevent introduction of bias?**	Yes
5.1.	In intervention study, were subjects, clinicians/practitioners, and investigators blinded to treatment group, as appropriate?	N/A
5.2.	Were data collectors blinded for outcomes assessment? (If outcome is measured using an objective test, such as a lab value, this criterion is assumed to be met.)	Yes
5.3.	In cohort study or cross-sectional study, were measurements of outcomes and risk factors blinded?	Yes
5.4.	In case control study, was case definition explicit and case ascertainment not influenced by exposure status?	N/A
5.5.	In diagnostic study, were test results blinded to patient history and other test results?	N/A
6.	**Were intervention/therapeutic regimens/exposure factor or procedure and any comparison(s) described in detail? Were interveningfactors described?**	Yes
6.1.	In RCT or other intervention trial, were protocols described for all regimens studied?	N/A
6.2.	In observational study, were interventions, study settings, and clinicians/provider described?	Yes
6.3.	Was the intensity and duration of the intervention or exposure factor sufficient to produce a meaningful effect?	Yes
6.4.	Was the amount of exposure and, if relevant, subject/patient compliance measured?	N/A

6.5.	Were co-interventions (e.g., ancillary treatments, other therapies) described?	N/A
6.6.	Were extra or unplanned treatments described?	N/A
6.7.	Was the information for 6.4, 6.5, and 6.6 assessed the same way for all groups?	N/A
6.8.	In diagnostic study, were details of test administration and replication sufficient?	N/A
7.	**Were outcomes clearly defined and the measurements valid and reliable?**	???
7.1.	Were primary and secondary endpoints described and relevant to the question?	Yes
7.2.	Were nutrition measures appropriate to question and outcomes of concern?	Yes
7.3.	Was the period of follow-up long enough for important outcome(s) to occur?	Yes
7.4.	Were the observations and measurements based on standard, valid, and reliable data collection instruments/tests/procedures?	???
7.5.	Was the measurement of effect at an appropriate level of precision?	Yes
7.6.	Were other factors accounted for (measured) that could affect outcomes?	Yes
7.7.	Were the measurements conducted consistently across groups?	N/A
8.	**Was the statistical analysis appropriate for the study design and type of outcome indicators?**	Yes
8.1.	Were statistical analyses adequately described and the results reported appropriately?	Yes
8.2.	Were correct statistical tests used and assumptions of test not violated?	Yes
8.3.	Were statistics reported with levels of significance and/or confidence intervals?	Yes
8.4.	Was "intent to treat" analysis of outcomes done (and as appropriate, was there an analysis of outcomes for those maximally exposed or a dose-response analysis)?	N/A
8.5.	Were adequate adjustments made for effects of confounding factors that might have affected the outcomes (e.g., multivariate analyses)?	Yes
8.6.	Was clinical significance as well as statistical significance reported?	Yes
8.7.	If negative findings, was a power calculation reported to address type 2 error?	N/A
9.	**Are conclusions supported by results with biases and limitations taken into consideration?**	Yes
9.1.	Is there a discussion of findings?	Yes

	9.2.	Are biases and study limitations identified and discussed?	Yes
10.	**Is bias due to study's funding or sponsorship unlikely?**		Yes
	10.1.	Were sources of funding and investigators' affiliations described?	Yes
	10.2.	Was the study free from apparent conflict of interest?	Yes